**PATENT IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

First Applicant: LUDWIG Dale L.
Patent No.: 7,638,605
Issue Date: December 29, 2009
Serial No.: 10/555407
Filed: May 3, 2004
PCT Nat'l Entry Date (if applicable): November 1, 2005
371 Date: June 8, 2007
Title: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR
Docket No.: X18524

Group Art Unit: 1643
Examiner: Blanchard, David J

**REQUEST FOR RECONSIDERATION OF PATENT TERM ADJUSTMENT INDICATED AT ISSUANCE (37 C.F.R. § 1.705(d))**

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentee submits this Request for Reconsideration of Patent Term Adjustment under 37 C.F.R. § 1.705(d) in the above-referenced issued patent, accompanied by the requisite fee under 37 C.F.R. § 1.18(e). Patentee believes that no additional fees are due with the filing of this Request. However, if any fees are required, Patentee hereby authorizes the Commissioner to charge such fee, or credit any overpayment in fees, to Deposit Account No. 05-0840.

**REMARKS**

Patentee hereby petitions the U.S. Patent and Trademark Office for reconsideration of the Patent Term Adjustment ("PTA") calculation. Applicants received Notice of Issuance from the U.S. Patent and Trademark Office, mailed on December 9, 2009, with notification that the Patent Term Adjustment under 35 U.S.C. §154(b) is 263 days. It is the Patentee's position that the PTA calculation should be amended to 455 days based on the facts provided herein. This PTA request is

submitted in view of the decision by the U.S. Court of Appeals for the Federal Circuit in *Wyeth v. Kappos*, 591 F.3d 1364 (Fed. Cir., 2010) and the "Notice Concerning Calculation of the Patent Term Adjustment under 35 U.S.C. § 154(b)(1)(B) involving International Applications Entering the National Stage Pursuant to 35 U.S.C. § 371" issued on September 9, 2009.

There are no issues that were raised or could have been raised in the application pertaining to patent term adjustment under 37 C.F.R § 1.705(b) before the patent issued. This request for patent term adjustment raises new issues that could only be raised following the issuance of the patent, which fully complies with 37 C.F.R § 1.705(b)(2)(iv)(A). This petition is filed within two months of the date the patent issued in accordance with 37 C.F.R § 1.705(d).

## BACKGROUND

According to the provisions of 35 U.S.C. § 154(b)(1)(B) and 37 C.F.R. § 1.702(b), Applicants are entitled to PTA for the failure of the Office to issue a patent within three years after the actual filing date of the application in the United States. Pendency of the application should be measured from the filing date which is the date that "the national stage" commenced under 35 U.S.C. § 371(b) or (f). Delays in prosecution legitimately attributable to applicant or failure of the applicant to engage in reasonable efforts to conclude processing or examination of the application as set forth in 37 C.F.R. § 1.704(b) should be subtracted from the total PTA calculation. A patentee is entitled to both "A Delay" and "B Delay" to the extent that the "A Delay" and "B Delay" terms do not occur on the same calendar day. *Wyeth v. Kappos*, 591 F.3d 1364, 1370 (Fed. Cir., 2010).

## STATEMENT OF FACTS

1. The present application is a national stage filing under 35 U.S.C. § 371 of international application number PCT/US2004/013852, filed May 3, 2004, claiming priority of U.S. Provisional Application No. 60/467,177, filed May 1, 2003. *See* Exhibit 2.

2. The national stage for the present application was filed on November 1, 2005. *See* Exhibit 2.
3. A notice of missing parts regarding the oath/declaration was mailed on January 16, 2007. *See* Exhibit 3.
4. The response to the notice of missing parts was filed on June 8, 2007. *See* Exhibits 1 and 4.
5. The requirements of 35 U.S.C. § 371 were fulfilled on June 8, 2007. *See* Exhibits 1 and 4.
6. The PTO mailed the first non-final Office Action on April 28, 2009. *See* Exhibits 1 and 5.
7. The Notice of Allowance was mailed on August 10, 2009. *See* Exhibits 1 and 6.
8. The Notice of Allowance cited 263 days of PTA. *See* Exhibit 6.
9. The Issue Fee was paid on November 10, 2009. *See* Exhibits 1 and 7.
10. Notice of Issuance mailed on the December 9, 2009, with notification that the Patent Term Adjustment is 263 days. *See* Exhibits 1 and 8.
11. US Patent No. 7,638,605 issued on December 29, 2009. *See* Exhibits 1 and 8.

**THE ACTUAL FILING DATE OF A U.S. NATIONAL STAGE APPLICATION FILED UNDER 35 U.S.C. § 371 IS 30 MONTHS FROM THE PRIORITY DATE**

Patentee respectfully submits that the Office did not apply the proper standard for determining the period of "B Delay" under 35 U.S.C. § 154(b)(1)(B). It is the patentee's understanding that the Office measured application pendency as beginning on June 8, 2007, the date on which the application fulfilled the requirements of 35 U.S.C. § 371. However, as detailed below, the relevant statutes and regulations state that when calculating "B Delay" for a national stage filing under 35 U.S.C. § 371, application pendency must be measured from the date that is 30 months from the priority date of the international application, not from the date on which the application fulfilled the requirements of 35 U.S.C. § 371 as stated in the "Notice Concerning Calculation of the Patent Term Adjustment under 35 U.S.C. § 154(b)(1)(B) involving International Applications Entering the National Stage Pursuant to 35 U.S.C. § 371" issued on September 9, 2009.

The term of a patent shall be extended if the Office fails to issue a patent within three years after the "actual filing date" of the application.

> Subject to the limitations under paragraph (2), if the issue of an original patent is delayed due to the failure of the United States Patent and Trademark Office to issue a patent within 3 years after the actual filing date of the application in the United States . . . the term of the patent shall be extended 1 day for each day after the end of that 3-year period until the patent is issued.

35 U.S.C. § 154 (b)(l)(B) (emphasis added). 37 C.F.R. §1.702(b) explains the meaning of the term "actual filing date" as set forth in 35 U.S.C. § 154(b)(l)(B). As detailed below, PTO delay for a national stage application begins if the Office fails to issue a patent within three years after the date the national stage "commenced under 35 U.S.C. 371(b) or (f)."

> *Failure to issue a patent within three years of the actual filing date of the application.* Subject to the provisions of 35 U.S.C. 154(b) and this subpart, the term of an original patent shall be adjusted if the issuance of the patent was delayed due to the failure of the Office to issue a patent within three years after the date on which the application was filed under 35 U.S.C. 111(a) or the national stage commenced under 35 U.S.C. 371(b) or (f) in an international application...

37 C.F.R. § 1.702(b) (emphasis added).

35 U.S.C. § 371(b) states that a national stage application "commences" "with the expiration of the applicable time limit under article 22 (1) or (2), or under article 39 (l)(a) of the treaty." 35 U.S.C. § 371 (f) states that "at the express request of the applicant, the national stage of processing may be commenced at any time at which the application is in order for such purpose and the applicable requirements of subsection (c) of this section have been complied with."

In the instant case, Applicants filed under 35 U.S.C. § 371(b). Under the provisions of 35 U.S.C. § 371(b), the U.S. national stage commences after the expiration of the applicable time limit under article 22(1) or (2), or under article 39(l)(a) of the treaty. The "applicable time limit" referred to in Patent Cooperation Treaty articles 22(1), 22(2), and 39(l)(a) is "the expiration of 30 months from the priority date."

> [I]n the absence of an express request for early processing of an international application under 35 U.S.C. 371(f) and compliance with the conditions provided therein, the U.S. national stage will commence upon expiration of 30 months from the priority date of the international application.

MPEP § 1893.01 (emphasis added).

It appears that in a similar petition filed in U.S. Patent 7,465,444, the Office recognized that for the purposes of calculating "B Delay" for a national stage filing under 35 U.S.C. § 371, application pendency is measured from the date that is 30 months from the priority date of the international application. *See* Exhibit 9, "Decision On Request For Reconsideration of Patent Term Adjustment" page 2 paragraph 4.

**B DELAY IS CALCULATED FROM THE "ACTUAL FILING DATE"**

The patentee respectfully submits that the "actual filing date" of a U.S. national stage application filed under 35 U.S.C. § 371(b), for purposes of calculating "B Delay" under 35 U.S.C. § 154(b)(l)(B) and 37 C.F.R. § 1.702(b), is the date that is 30 months from the priority date of the international application. Accordingly, the actual filing date of U.S. Patent No. 7,638,605 is November 1, 2005. Therefore, the "actual filing date" for purposes of calculating "B Delay" in the instant application should be revised from June 8, 2007 to November 1, 2005.

The patentee respectfully requests that the "B Delay" be recalculated to account for the foregoing, in light of the decision by the U.S. Court of Appeals for the Federal Circuit decision in *Wyeth v. Kappos*, 591 F.3d 1364 (Fed. Cir., 2010) and the "Notice Concerning Calculation of the Patent Term Adjustment under 35 U.S.C. § 154(b)(1)(B) involving International Applications Entering the National Stage Pursuant to 35 U.S.C. § 371". The Federal Circuit in *Wyeth* held that a patentee is entitled to both "A Delay" and "B Delay" to the extent that the "A Delay" and "B Delay" terms do not occur on the same calendar day. *See id.* at 1370. Since the above referenced application was filed on November 1, 2005 and did not issue until December 29, 2009, this application was pending longer than three years after the actual filing date. "B Delay" should therefore be recalculated as set forth below in accordance with 35 U.S.C. § 154 (b)(l)(B).

**REVIEW AND RECALCULATION OF PATENT TERM ADJUSTMENT**

**"A DELAY"**

The PTO calculated an "A Delay" of 263 days. Applicant does not dispute this calculation. A first PTO action mailed on or after August 9, 2008, the day after the date that is fourteen months after the date on which the application fulfilled the requirements of 35 U.S.C. § 371 (which in the instant case is June 8, 2007), would trigger the start of the "A Delay." *See* 37 C.F.R. § 1.703(a)(1). In the instant case, the PTO mailed the first non-final Office Action on April 28, 2009, thereby accumulating a PTO Delay of 263 days. Accordingly, the patentee agrees that the "A Delay" calculated by the PTO from the period beginning August 9, 2008 (the day after the end of the fourteen month deadline) to April 28, 2009 was correctly determined by the PTO to be 263 days.

**"B DELAY"**

The "B Delay" in the instant patent should be 423 days. The present patent issued from an application that is a national stage filing under 35 U.S.C. § 371 of international application number PCT/US2004/013852, filed May 3, 2004, which claims priority of U.S. Provisional Application No. 60/467,177, filed May 1, 2003. First, the national stage for the present patent "commenced" under the provisions of 35 U.S.C. § 371(b), on November 1, 2005, which is 30 months from the priority date of May 1, 2003. *See* 35 U.S.C. § 154(b)(1)(B).

"B Delay" commenced on November 2, 2008, the day after three years from the actual filing date of November 1, 2005, and ended on the date the patent issued, December 29, 2009. *See* 37 C.F.R. § 1.703(b). This term is 423 days in length.

The PTO incorrectly calculated the "B Delay" term based on the fulfillment of the 35 C.F.R. § 371 obligations, rather than from the actual filing date of the application as required by 37 C.F.R. § 1.702(b). As a result, the PTO's calculation of "B Delay" is incorrect and lead to an erroneous finding of 0 days of "B Delay." The correct PTO "B Delay" for issuance of the patent after three years from filing is 423 days. *See* 37 C.F.R. §§ 1.702(b) and 1.703(b).

## OVERLAP OF "A DELAY" AND "B DELAY"

As detailed above, "A Delay" accumulated during the following period: August 09, 2008, to April 28, 2009. This is a total of 263 days.

As detailed above, "B Delay" accumulated during the following period: November 02, 2008, to December 29, 2009. This is a total of 423 days.

The "A Delay" and "B Delay" terms overlap from November 02, 2008 to April 28, 2009. This is a total of 178 days.

## APPLICANT DELAY

Delay in submitting an oath or declaration in response to a Notice of Missing Parts could constitute a failure to engage in reasonable efforts to conclude processing or examination of the application as set forth 37 C.F.R. § 1.704.

> With respect to the grounds for adjustment set forth in §§ 1.702(a) through (e), and in particular the ground of adjustment set forth in § 1.702(b), an applicant shall be deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application for the cumulative total of any periods of time in excess of three months that are taken to reply to any notice or action by the Office making any rejection, objection, argument, or other request, measuring such three-month period from the date the notice or action was mailed or given to the applicant, in which case the period of adjustment set forth in § 1.703 shall be reduced by the number of days, if any, beginning on the day after the date that is three months after the date of mailing or transmission of the Office communication notifying the applicant of the rejection, objection, argument, or other request and ending on the date the reply was filed. The period, or shortened statutory period, for reply that is set in the Office action or notice has no effect on the three-month period set forth in this paragraph.

37 C.F.R. § 1.704(b). A notice of missing parts was mailed on January 16, 2007. Under 37 C.F.R. § 1.704, applicants were required to respond to the objection by April 16, 2007 which corresponds to three months from the notice. The response to the notice of missing parts was filed on June 8, 2007. A period of 53 days occurred between April 17, 2007, the day following the three month response period, and June 8, 2007, the date of filing of the oath / declaration.

## TERMINAL DISCLAIMER

This patent is not subject to a terminal disclaimer.

## TOTAL PTA

Total PTA should be calculated as 455 days, *not* 263 days:

1) Total PTO Delay should be calculated as 508 days. This represents the sum of 263 days of 37 C.F.R. § 1.702(a) or "A Delay" and 423 days of 37 C.F.R. § 1.702(b) or "B Delay" minus 178 days of overlapping "A Delay" and "B Delay");
2) Total PTO Delay under 37 C.F.R. § 1.702(c)-(e) should be calculated as 0 days;
3) Total Applicant Delay under 37 C.F.R. § 1.704 should be calculated as 53 days; and
4) Total PTA should be calculated as 455 days. This represents 508 days of PTO Delay minus 53 days of Applicant Delay.

## CONCLUSION

In consideration of the events described above, and in light of the recent Federal Circuit *Wyeth* decision and the "Notice Concerning Calculation of the Patent Term Adjustment under 35 U.S.C. § 154(b)(1)(B) involving International Applications Entering the National Stage Pursuant to 35 U.S.C. § 371", the total PTA calculation should be 455 days, not 263 days. As such, Patentee respectfully requests reconsideration of the PTA.

Respectfully submitted,

/Nicole S. Woods/
Nicole S. Woods
Attorney for Applicant
Registration No. 56,579
Phone: 908-203-6835

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

February 26, 2010

# Exhibit 1

## Transaction History

| Date | Transaction Description |
|---|---|
| 02-02-2010 | Sequence Moved to Public Database |
| 12-29-2009 | Recordation of Patent Grant Mailed |
| 12-10-2009 | Email Notification |
| 12-09-2009 | Issue Notification Mailed |
| 12-29-2009 | Patent Issue Date Used in PTA Calculation |
| 11-13-2009 | Dispatch to FDC |
| 11-13-2009 | Application Is Considered Ready for Issue |
| 11-10-2009 | Issue Fee Payment Verified |
| 11-10-2009 | Issue Fee Payment Received |
| 08-24-2009 | Sequence Forwarded to Pubs on Tape |
| 08-11-2009 | Electronic Review |
| 08-10-2009 | Email Notification |
| 08-10-2009 | Email Notification |
| 08-10-2009 | Mail Examiner's Amendment |
| 08-10-2009 | Mail Notice of Allowance |
| 08-04-2009 | Document Verification |
| 08-04-2009 | Notice of Allowance Data Verification Completed |
| 08-04-2009 | Case Docketed to Examiner in GAU |
| 08-03-2009 | Examiner's Amendment Communication |
| 08-03-2009 | Email Notification |
| 08-03-2009 | Mail Examiner Interview Summary (PTOL - 413) |
| 07-28-2009 | Examiner Interview Summary Record (PTOL - 413) |
| 12-23-2008 | Information Disclosure Statement considered |
| 12-23-2008 | Information Disclosure Statement considered |
| 05-29-2009 | Date Forwarded to Examiner |
| 05-28-2009 | Response to Election / Restriction Filed |
| 04-28-2009 | Electronic Review |
| 04-28-2009 | Email Notification |
| 04-28-2009 | Mail Restriction Requirement |
| 04-24-2009 | Requirement for Restriction / Election |
| 12-23-2008 | Electronic Information Disclosure Statement |
| 12-23-2008 | Electronic Information Disclosure Statement |
| 03-12-2009 | Email Notification |
| 03-12-2009 | Change in Power of Attorney (May Include Associate POA) |
| 03-06-2009 | Correspondence Address Change |
| 12-23-2008 | Information Disclosure Statement (IDS) Filed |
| 12-23-2008 | Information Disclosure Statement (IDS) Filed |
| 06-25-2008 | Change in Power of Attorney (May Include Associate POA) |
| 06-24-2008 | Correspondence Address Change |
| 03-01-2008 | Case Docketed to Examiner in GAU |
| 11-01-2005 | Request for Foreign Priority (Priority Papers May Be Included) |
| 01-31-2008 | PG-Pub Issue Notification |
| 11-01-2007 | Miscellaneous Incoming Letter |
| 11-01-2005 | Preliminary Amendment |
| 11-11-2007 | Application Dispatched from OIPE |
| 10-31-2007 | Change in Power of Attorney (May Include Associate POA) |
| 10-25-2007 | Correspondence Address Change |

| | |
|---|---|
| 06-08-2007 | 371 Completion Date |
| 08-21-2007 | Sent to Classification Contractor |
| 08-21-2007 | Notice of DO/EO Acceptance Mailed |
| 06-08-2007 | Additional Application Filing Fees |
| 06-08-2007 | A statement by one or more inventors satisfying the requirement under 35 USC 115, Oath of the Applic |
| 05-18-2006 | Cleared by OIPE CSR |
| 11-17-2005 | CRF Is Good Technically / Entered into Database |
| 11-01-2005 | CRF Disk Has Been Received by Preexam / Group / PCT |
| 11-01-2005 | Initial Exam Team nn |

Close Window

# Exhibit 2

FORM PTO-1390 (REV. 10-2003) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 11245/53202

U.S. APPLICATION NO. (If known, see 37 CFR 1.5): To Be Assigned 10/555407

| INTERNATIONAL APPLICATION NO. | INTERNATIONAL FILING DATE | PRIORITY DATE CLAIMED: |
|---|---|---|
| PCT/US2004/013852 | 03 May 2004 | 01 May 2003 |

TITLE OF INVENTION

FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

APPLICANT(S) FOR DO/EO/US

Dale L. LUDWIG

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☑ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☑ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☑ The US has been elected (Article 31).
5. ☑ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☐ has been communicated by the International Bureau.
   c. ☑ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☑ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (Unsigned)
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11 to 20 below concern document(s) or information included:**

11. ☑ Preliminary Amendment.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An Application Data Sheet under 37 CFR 1.76.
15. ☐ A substitute specification.
16. ☐ A power of attorney and/or change of address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13*ter*.2 and 37 CFR 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☑ Other items or information: Copy of Published International Application; copy of International Search Report; Sequence Listing in paper form (eighteen(18) pages) and computer readable form (one(1) diskette); Sequence Listing Statement



EXPRESS MAIL NO. EV 321894506 US

| U.S. APPLICATION NO. (if known, see 37 CFR 1.5) To Be Assigned 10/555407 | INTERNATIONAL APPLICATION NO. PCT/US2004/013852 | ATTORNEY'S DOCKET NUMBER 11245/53202 | |
|---|---|---|---|
| The following fees are submitted: | | | |
| 21 ☐ **Basic National Fee** | $ 300.00 | $300.00 | |
| 22. ☐ **Examination Fee** – If International preliminary exam report prepared by USPTO and all claims satisfy provisions of PCT Article 33/(1)-(4) | $ 100.00 | $ | |
| ☐ Examination Fee - All other situations | $ 200.00 | $200.00 | |
| 23. ☐ **Search Fee** – Search fee (37 CFR 1.445(a)(2) has been paid on the international application to the USPTO as ISA | $ 100.00 | $ | |
| ☐ International Search Report prepared and provided to the Office | $ 400.00 | $400.00 | |
| ☐ Search Fee – All other situations | $ 500.00 | $ | |
| **TOTAL OF ABOVE CALCULATIONS** | | $900.00 | |

☐ Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing on computer program listing filed in an electronic medium). The fee is $250 for each additional 50 sheets of paper or fraction thereof.

| Total Sheets | Extra Sheets | Number of each additional 50 or fraction thereof (round up to a whole number) | RATE | | |
|---|---|---|---|---|---|
| -100 | /50= | 1 | x $250 | | |
| Surcharge of $130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)). | | | | $ | |

| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE | | |
|---|---|---|---|---|---|
| Total Claims | 73 - 20 = | 53 | x $50.00 | 2,650.00 | |
| Independent Claims | 5 - 3 = | 2 | x $200.00 | $400.00 | |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | + $360.00 | $360.00 | |
| | | **TOTAL OF ABOVE CALCULATIONS =** | | $ | |
| ☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. | | | | | |
| | | | **SUBTOTAL =** | $4,310.00 | |
| Processing fee of $130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | | $ | |
| | | | **TOTAL NATIONAL FEE =** | $4,310.00 | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property | | | | $ | |
| | | | **TOTAL FEES ENCLOSED =** | $4,310.00 | |
| | | | **Amount to be refunded:** | $ | |
| | | | **Amount to be charged** | $ | |

a. ☐ A check in the amount of $_____ to cover the above fees is enclosed.

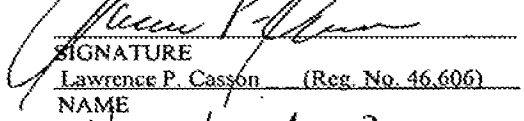
b. ☑ Please charge my Deposit Account No. 11-0600 in the amount of $4,310.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☑ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-0600. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

**NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.**

SEND ALL CORRESPONDENCE TO:
KENYON & KENYON
One Broadway
New York, New York 10004
**CUSTOMER NO. 26646**



SIGNATURE
Lawrence P. Casson (Reg. No. 46,606)
NAME
November 1, 2005
DATE



EXPRESS MAIL NO. EV 321894506 US

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 February 2005 (24.02.2005)

PCT

(10) International Publication Number
WO 2005/016970 A2

(51) International Patent Classification[7]: C07K 16/28, A61K 39/395, A61P 35/00, C12N 15/13, 15/63, 5/10

(21) International Application Number: PCT/US2004/013852

(22) International Filing Date: 3 May 2004 (03.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/467,177 1 May 2003 (01.05.2003) US

(71) Applicant *(for all designated States except US)*: **IMCLONE SYSTEMS INCORPORATED** [US/US]; 180 Varick Street, New York, NY 10014 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **LUDWIG, Dale, L.** [US/US]; 14 Lookout Road, Randolph, NJ 07869 (US).

(74) Agents: **SOMERVILLE, Deborah, A.** et al.; Kenyon & Kenyon, One Broadway, New York, NY 10004 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**
— *without international search report and to be republished upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

(57) Abstract: This invention relates to human antibodies that bind to human insulin-like growth factor-1 receptor (IGF-IR), to derivatives of these antibodies (Fabs, single chain antibodies, bi-specific antibodes, or fusion proteins), and to uses of the antibodies and derivatives in therapeutic, and diagnostic methods. The invention relates to nucleic acids encoding the anti-IGF-IR, methods of generating the antibodies and expression. The invention further relates to combination therapies using ant-IGF-IR antibodies with anti-neoplastic drugs.

WO 2005/016970 A2

# FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

[0001] This application claims the benefit of United States Provisional Application 60/467,177, filed May 1, 2003.

## BACKGROUND

[0002] The insulin-like growth factor receptor (IGF-IR) is a ubiquitous transmembrane tyrosine kinase receptor that is essential for normal fetal and post-natal growth and development. IGF-IR can stimulate cell proliferation, cell differentiation, changes in cell size, and protect cells from apoptosis. It has also been considered to be quasi-obligatory for cell transformation (reviewed in Adams et al., *Cell. Mol. Life Sci.* 57:1050-93 (2000); Baserga, *Oncogene* 19:5574-81 (2000)). The IGF-IR is located on the cell surface of most cell types and serves as the signaling molecule for growth factors IGF-I and IGF-II (collectively termed henceforth IGFs). IGF-IR also binds insulin, albeit at three orders of magnitude lower affinity than it binds to IGFs. IGF-IR is a pre-formed hetero-tetramer containing two alpha and two beta chains covalently linked by disulfide bonds. The receptor subunits are synthesized as part of a single polypeptide chain of 180kd, which is then proteolytically processed into alpha (130kd) and beta (95kd) subunits. The entire alpha chain is extracellular and contains the site for ligand binding. The beta chain possesses the transmembrane domain, the tyrosine kinase domain, and a C-terminal extension that is necessary for cell differentiation and transformation, but is dispensable for mitogen signaling and protection from apoptosis.

[0003] IGF-IR is highly similar to the insulin receptor (IR), particularly within the beta chain sequence (70% homology). Because of this homology, recent studies have demonstrated that these receptors can form hybrids containing one IR dimer and one IGF-IR dimer (Pandini et al., *Clin. Canc. Res.* 5:1935-19 (1999)). The formation of hybrids occurs in both normal and transformed cells and the hybrid content is dependent upon the concentration of the two homodimer receptors (IR and IGF-IR) within the cell. In one study of 39 breast cancer specimens, although both IR and IGF-IR were over-expressed in all tumor samples, hybrid receptor content consistently exceeded the levels of both homo-receptors by approximately 3-fold (Pandini et al., *Clin. Canc. Res.* 5:1935-44 (1999)). Although hybrid receptors are composed of IR and IGF-IR pairs, the hybrids bind selectively to IGFs, with

# Exhibit 3

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| U.S. APPLICATION NUMBER NO. | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
|---|---|---|
| 10/555,407 | Dale L. Ludwig | 11245/53202 |

| INTERNATIONAL APPLICATION NO. | |
|---|---|
| PCT/US04/13852 | |
| I.A. FILING DATE | PRIORITY DATE |
| 05/03/2004 | 05/01/2003 |

26646
KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004

**CONFIRMATION NO. 7544**

**371 FORMALITIES LETTER**

*OC000000021999062*

Date Mailed: 01/16/2007

## NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 11/01/2005
- Copy of the International Search Report filed on 11/01/2005
- Preliminary Amendments filed on 11/01/2005
- Biochemical Sequence Diskette filed on 11/01/2005
- Biochemical Sequence Listing filed on 11/01/2005
- Request for Immediate Examination filed on 11/01/2005
- U.S. Basic National Fees filed on 11/01/2005
- Priority Documents filed on 11/01/2005

The applicant needs to satisfy supplemental fees problems indicated below.

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.

- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.492(h) of $130 for a non-small entity, must be submitted with the missing items identified in this letter.

SUMMARY OF FEES DUE:

Total additional fees required for this application is **$130** for a Large Entity:

- **$130** Surcharge.

**ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.**

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web.
https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

**If you are not using EFS-Web to submit your reply, you must include a copy of this notice.**

LAMONT M HUNTER

Telephone: (703) 308-9140 EXT 201

PART 2 - OFFICE COPY

| U.S. APPLICATION NUMBER NO. | INTERNATIONAL APPLICATION NO. | ATTY. DOCKET NO. |
|---|---|---|
| 10/555,407 | PCT/US04/13852 | 11245/53202 |

FORM PCT/DO/EO/905 (371 Formalities Notice)

# Exhibit 4

FORM PTO-1390 (Modified) U.S. PATENT AND TRADEMARK OFFICE; U.S. DEPARTMENT OF COMMERCE
(REV. 5-2003)

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371

| ATTORNEY'S DOCKET NUMBER | |
|---|---|
| 1017.53202 | |
| U.S. APPLICATION NO. (If known, see 37 CFR 1.5) | |
| 10/555,507 | |

| INTERNATIONAL APPLICATION NO. | INTERNATIONAL FILING DATE | PRIORITY DATE CLAIMED |
|---|---|---|
| PCT/US2004/013852 | 3 May 2004 | 1 May 2003 |

TITLE OF INVENTION
**FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR**

APPLICANT(S) FOR DO/EO/US
**Dale L. Ludwig**

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☐ This is a **FIRST** submission of items concerning a submission under 35 U.S.C. 371.
2. ☒ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a submission under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (25) indicated below.
4. ☐ The US has been elected (Article 31).
5. ☐ A copy of the International Application as filed (35 U.S.C. 371 (c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☐ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A copy of the International Search Report (PCT/ISA/210).

**Items 13 to 23 below concern document(s) or information included:**

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ An Application Data Sheet under 37 CFR 1.76.
18. ☐ A substitute specification.
19. ☐ A power of attorney and/or change of address letter.
20. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13*ter*.2 and 37 CFR 1.821 - 1.825.
21. ☐ A second copy of the published International Application under 35 U.S.C. 154(d)(4).
22. ☐ A second copy of the English language translation of the International Application under 35 U.S.C. 154(d)(4).
23. ☐ Express Mail Label No.

| U.S. APPLICATION NO (if known, see 37 CFR 1.5) | INTERNATIONAL APPLICATION NO. | ATTORNEY'S DOCKET NUMBER |
|---|---|---|
| | PCT/US2004/013852 | |

24. Other items or information:

**Petition for Three Month Extension (1 page)**
**Note change of attorney from Kenyon to Lucas & Mercanti, LLP by Power of Attorney**

| The following fees have been submitted: | CALCULATIONS | PTO USE |
|---|---|---|
| 26. ☐ Basic national fee (37 CFR 1.492(a)). . . . . $300 | $ $0.00 | |
| 26. ☐ Examination fee (37 CFR 1.492(c))<br>If the written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4). $0<br>All other situations. . . . . $200 | $ $0.00 | |
| 27. ☐ Search fee (37 CFR 1.492(b))<br>If the written opinion of the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4). . . . $0<br>Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority. . . . . $100<br>International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB. . . . . $400<br>All other situations. . . . . $500 | $ $0.00 | |
| **TOTAL OF 25, 26 and 27 =** | $ $0.00 | |
| ☐ Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing in compliance with 37 CFR 1.821(c) or (e) in an electronic medium or computer program listing in an electronic medium) (37 CFR 1.492(j)).<br>The fee is $250 for each additional 50 sheets of paper or fraction thereof. | | |
| Total Sheets: - 100 = 0 / 50 = | Extra Sheets: 0 | Number of each additional 50 or fraction thereof (round up to a whole): 0 — RATE: × $250.00 |
| | $ $0.00 | |
| Surcharge of $130.00 for furnishing any of the search fee, examination fee, or the oath or declaration after the date of commencement of the national stage (37 CFR 1.492(h)). | $ $130.00 | |

| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE | CALCULATIONS | PTO USE |
|---|---|---|---|---|---|
| Total claims | - 20 = | 0 | × $50.00 | $ $0.00 | |
| Independent claims | - 3 = | 0 | × $200.00 | $ $0.00 | |
| MULTIPLE DEPENDENT CLAIMS (if applicable) | ☐ | | + $360.00 | $ $0.00 | |
| **TOTAL OF ABOVE CALCULATIONS =** | | | | $ $130.00 | |
| ☐ Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by 1/2. | | | | $ $0.00 | |
| **SUBTOTAL =** | | | | $ $130.00 | |
| Processing fee of $130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | | $ $0.00 | |
| **TOTAL NATIONAL FEE =** | | | | $ $130.00 | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40 per property + | | | | $ $0.00 | |
| **TOTAL FEES ENCLOSED =** | | | | $ $130.00 | |
| | | | | Amount to be | $ |
| | | | | Amount to be | $ |

a. ☐ A check in the amount of $ _____ to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-2275 . A duplicate copy of this sheet is enclosed.

d. ☒ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038. The PTO-2038 should only be mailed or faxed to the USPTO. However, when paying the basic national fee, the PTO-2038 may NOT be faxed to the USPTO.

**ADVISORY:** If filing by EFS-Web, do **NOT** attach the PTO-2038 form as a PDF along with your EFS-Web submission. Please be advised that this is **not** recommended and by doing so your **credit card information may be displayed via PAIR.** To

**NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.**

SEND ALL CORRESPONDENCE TO:

**Customer No. 20311**
**LUCAS & MERCANTI, LLP**
**475 Park Avenue South**
**New York, New York 10016**
**Phone: 212-661-8000**
**Fax: 212-661-8002**

SIGNATURE

**Michael N. Mercanti**
NAME

**33,966**
REGISTRATION NUMBER

**June 8, 2007**
DATE

| PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) (Large Entity) | Docket No. 1017.53202 |
|---|---|

In Re Application Of: **Dale L. Ludwig**

| Application No. | Filing Date | Examiner | Customer No. | Group Art Unit | Confirmation No. |
|---|---|---|---|---|---|
| 10/555,407 | 05/03/2004 | Unknown | 20311 | Unknown | 7544 |

Invention: **FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR**

COMMISSIONER FOR PATENTS:

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a response to the Office Action of 01/16/2007 (Date) in the above-identified application.

The requested extension is as follows (check time period desired):

☐ One month ☐ Two months ☒ Three months ☐ Four months ☐ Five months

from: March 16, 2007 (Date) until: June 16, 2007 (Date)

The fee for the extension of time is $1,020 and is to be paid as follows:

☐ A check in the amount of the fee is enclosed.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. 02-2275

☒ If an additional extension of time is required, please consider this a petition therefor and charge any additional fees which may be required to Deposit Account No. 02-2275

☒ Payment by credit card. Form PTO-2038 is attached.

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

Signature

Dated: June 8, 2007

Michael N. Mercanti
Reg. No. 33,966
LUCAS & MERCANTI, LLP
475 Park Avenue South
New York, New York 10016
Phone: 212-661-8000
Fax: 212-661-8002

CERTIFICATE OF ELECTRONIC TRANSMISSION
I hereby certify that this document is being electronically transmitted to the Commissioner for Patents via EFS-Web on June 8, 2007.

LUCAS & MERCANTI, LLP

BY: Michael N. Mercanti

cc:

DOCKET NO. 1017.53202

## DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below; I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:
**FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR**

the specification of which (check only one item below):

_____ is attached hereto.

_X_ was filed as United States Application No. 10/555,507 or as PCT International Application No. _____ on November 1, 2005 and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me to be material to the examination of this application as defined by 37 CFR 1.56.

## FOREIGN AND DOMESTIC PRIORITY CLAIMS UNDER 35 USC 119 AND PRIOR FOREIGN/PCT APPLICATIONS

I hereby claim foreign or domestic priority benefits under 35 USC 119 `````or 365(b) for any United States provisional patent application or foreign application(s) for patent or inventor's or plant breeder's rights certificate(s) or under 35 USC 365(a) for any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's or plant breeder's rights certificate(s) or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

| COUNTRY/APPLICATION NO. (if PCT, indicate "PCT") | DATE OF FILING (day/month/year) | PRIORITY CLAIMED UNDER 35 USC 119 |
|---|---|---|
| 60/467,177 | 01/05/2003 | [X] YES [ ] NO |
| | | [ ] YES [ ] NO |
| | | [ ] YES [ ] NO |
| | | [ ] YES [ ] NO |

## PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 USC 120

I hereby claim the benefit under 35 USC 120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of 35 USC 112, I acknowledge the duty to disclose material information as defined in 37 CFR 1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

| PCT/US APPLICATION NO. | PCT/US FILING DATE | PATENTED | PENDING | ABANDONED |
|---|---|---|---|---|
| PCT/US2004/013852 | May 3, 2004 | [ ] | [X] | [ ] |
| | | [ ] | [ ] | [ ] |
| | | [ ] | [ ] | [ ] |
| | | [ ] | [ ] | [ ] |

## POWER OF ATTORNEY AND CORRESPONDENCE ADDRESS

I hereby appoint the following attorneys at the address listed below to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith and to receive all correspondence in connection with this application:

Donald C. Lucas, Registration No. 31,275
Michael N. Meredith, Registration No. 33,966

Laurence Manber, Registration No. 35,597
Otho B. Ross, Registration No. 32,754
Timothy Meade, Registration No. 55,449
Hyun Soon Cho, Registration No. L0306
Yaodong Chen, Registration No. L0267

ADDRESS: Lucas & Mercanti, LLP CUSTOMER NO. 20311
475 Park Avenue South
New York, NY 10016
Tel: 212-661-8000
Fax: 212-661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

## INVENTOR IDENTIFICATION AND SIGNATURE

FULL NAME OF SOLE OR FIRST Dale L. Ludwig

INVENTOR'S SIGNATURE _____ DATE 6/8/07

RESIDENCE Randolph, New Jersey CITIZENSHIP United States of American

POST OFFICE ADDRESS 14 Lookout Road, Randolph, New Jersey 07869

---

FULL NAME OF SECOND INVENTOR _____

INVENTOR'S SIGNATURE _____ DATE _____

RESIDENCE _____ CITIZENSHIP _____

POST OFFICE ADDRESS _____

---

FULL NAME OF THIRD INVENTOR _____

INVENTOR'S SIGNATURE _____ DATE _____

RESIDENCE _____ CITIZENSHIP _____

POST OFFICE ADDRESS _____

---

Cont....YES [ ] NO [X]

# Electronic Patent Application Fee Transmittal

| | |
|---|---|
| **Application Number:** | 10555407 |
| **Filing Date:** | |
| **Title of Invention:** | Fully human antibodies directed against the human insulin-like growth factor-1 receptor |
| First Named Inventor/Applicant Name: | Dale L. Ludwig |
| **Filer:** | Michael Nicholas Mercanti |
| **Attorney Docket Number:** | 11245/53202 |

Filed as Large Entity

## U.S. National Stage under 35 USC 371 Filing Fees

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| **Basic Filing:** | | | | |
| **Pages:** | | | | |
| **Claims:** | | | | |
| **Miscellaneous-Filing:** | | | | |
| Late filing fee for oath or declaration | 1051 | 1 | 130 | 130 |
| **Petition:** | | | | |
| **Patent-Appeals-and-Interference:** | | | | |
| Post-Allowance-and-Post-Issuance: | | | | |
| **Extension-of-Time:** | | | | |

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| Extension - 3 months with $0 paid | 1253 | 1 | 1020 | 1020 |
| **Miscellaneous:** | | | | |
| | | | **Total in USD ($)** | **1150** |

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 1855338 |
| **Application Number:** | 10555407 |
| **International Application Number:** | |
| **Confirmation Number:** | 7544 |
| **Title of Invention:** | Fully human antibodies directed against the human insulin-like growth factor-1 receptor |
| **First Named Inventor/Applicant Name:** | Dale L. Ludwig |
| **Customer Number:** | 26646 |
| **Filer:** | Michael Nicholas Mercanti |
| **Filer Authorized By:** | |
| **Attorney Docket Number:** | 11245/53202 |
| **Receipt Date:** | 08-JUN-2007 |
| **Filing Date:** | |
| **Time Stamp:** | 16:52:14 |
| **Application Type:** | U.S. National Stage under 35 USC 371 |

## Payment information:

| | |
|---|---|
| Submitted with Payment | no |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes) | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|
| 1 | Documents submitted with 371 Applications | Transmittal.pdf | 107001 | no | 3 |
| **Warnings:** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| **Information:** | | | | | |
| 2 | Extension of Time | PetitionforExtension.pdf | 35446 | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 3 | Miscellaneous Incoming Letter | NoticeofMissingParts.pdf | 47021 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 4 | Oath or Declaration filed | Declaration.pdf | 71105 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 5 | Fee Worksheet (PTO-06) | fee-info.pdf | 8361 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | **Total Files Size (in bytes):** | 268934 | | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**National Stage of an International Application under 35 U.S.C. 371**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**New International Application Filed with the USPTO as a Receiving Office**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NUMBER | FILING or 371(c) DATE | GRP ART UNIT | FIL FEE REC'D | ATTY.DOCKET.NO | TOT CLAIMS | IND CLAIMS |
|---|---|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | 1644 | 4440 | 11245/53202 | 56 | 5 |

**CONFIRMATION NO. 7544**

**FILING RECEIPT**

26646
KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY10004

Date Mailed: 08/21/2007

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

**Applicant(s)**

Dale L. Ludwig, Randolph, NJ;

**Power of Attorney:** The patent practitioners associated with Customer Number 26646

**Domestic Priority data as claimed by applicant**

This application is a 371 of PCT/US04/13852 05/03/2004
which claims benefit of 60/467,177 05/01/2003

**Foreign Applications**

**If Required, Foreign Filing License Granted:** 08/18/2007

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US10/555,407**

**Projected Publication Date:** 11/29/2007

**Non-Publication Request:** No

**Early Publication Request:** No

**Title**

Fully Human Antibodies Directed Against the Human Insulin-Like Growth Factor-1 Receptor

**Preliminary Class**

## PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

---

## LICENSE FOR FOREIGN FILING UNDER

## Title 35, United States Code, Section 184

## Title 37, Code of Federal Regulations, 5.11 & 5.15

**GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to

espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

# Exhibit 5

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | Dale L. Ludwig | X-18524 | 7544 |

23885 7590 04/28/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

| EXAMINER |
|---|
| BLANCHARD, DAVID J |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 04/28/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/555,407 | LUDWIG, DALE L. | |
| | Examiner | Art Unit | |
| | David J. Blanchard | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 November 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-56* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature recited in claim 1 is an isolated human antibody or fragment thereof that binds IGF-IR and has at least one property selected from the group consisting of (i) inhibits binding of IGF-I or IGF-II to IGF-IR, (ii) neutralizes activation of IGF-IR by IGF-I or IGF-II, (iii) reduces IGF-IR surface receptor expression by at least 80% and (iv) binds to IGF-IR with a $K_d$ of about 3 X $10^{-10}$ $M^{-1}$ or less. In view of this Cohen et al (US Patent 7,037,498, priority to 1/5/01, IDS reference 16 filed 12/23/08) reads on the claim. Cohen et al teach isolated human monoclonal antibodies that bind IGF-IR and inhibit binding of IGF-I or IGF-II to IGF-IR, neutralizes activation of IGF-IR by IGF-I or IGF-II and binds to IGF-IR with a $K_d$ of about 3 X $10^{-10}$ $M^{-1}$ or less (see entire document, particularly cols. 5-6, 8-10, 16-17 and 21). Therefore the technical feature recited in claim 1 is not special. Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-18 and 23-33, drawn to an isolated human antibody or fragment thereof that binds IGF-IR and pharmaceutical compositions comprising such.

Group II, claims 19-22, drawn to nucleic acid, vectors and host cells encoding human antibody or fragment thereof that binds IGF-IR.

Group III, claims 34 and 36-40, drawn to a method of treating acromegaly comprising administering a human antibody or fragment thereof that binds IGF-IR.

Group IV, claims 34 and 36-40, drawn to a method of treating retinal neovascularization comprising administering a human antibody or fragment thereof that binds IGF-IR.

Group V, claims 34 and 36-40, drawn to a method of treating psoriasis comprising administering a human antibody or fragment thereof that binds IGF-IR.

Group VI, claims 34, 37 and 41-56, drawn to a method of reducing tumor growth comprising administering a human antibody or fragment thereof that binds IGF-IR.

2. Claim 35 links inventions III-V. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 35.

Upon the indication of allowability of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

3. The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: As set forth above, in view of the teaching of Cohen

et al the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature of claim 1 is not special.

Inventions of Groups I-II represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The antibody of Group I and the polynucleotide of Group II are all structurally and chemically different from each other. The antibody is raised by immunization while the polynucleotide is made by nucleic acid synthesis. Furthermore, the polynucleotide can be used for hybridization screening and the antibody can be used to immunopurify the antigen, for example. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, the inventions I-II are patentably distinct.

The methods of Inventions III-VI differ in the method objectives. The Invention of Group III recites a method of treating acromegaly comprising administering a human antibody or fragment thereof that binds IGF-IR; Group IV recites a method of treating retinal neovascularization comprising administering a human antibody or fragment thereof that binds IGF-IR; Group V recites a method of treating psoriasis comprising administering a human antibody or fragment thereof that binds IGF-IR and Group VI recites a method of reducing tumor growth comprising administering a human antibody or fragment thereof that binds IGF-IR. Thus, the inventions of Groups III-VI are directed to methods of treating disorders having different etiologies and therapeutic endpoints and are not required one for the other. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, Inventions of Groups III-VI are separate and distinct in having different method objectives and different endpoints and are patentably distinct.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group I can be used in a materially different

method such as to immunopurify the antigen in addition to the materially different methods of Group III, IV, V and VI.

4. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;
(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
(d) the prior art applicable to one invention would not likely be applicable to another invention;
(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either

instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643

# Exhibit 6

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

# NOTICE OF ALLOWANCE AND FEE(S) DUE

23885 7590 08/10/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

| EXAMINER | |
|---|---|
| BLANCHARD, DAVID J | |
| ART UNIT | PAPER NUMBER |
| 1643 | |

DATE MAILED: 08/10/2009

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | Dale L. Ludwig | X-18524 | 7544 |

TITLE OF INVENTION: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|---|---|---|---|---|---|---|
| nonprovisional | NO | $1510 | $300 | $0 | $1810 | 11/10/2009 |

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

**HOW TO REPLY TO THIS NOTICE:**

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**



PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

# PART B - FEE(S) TRANSMITTAL

**Complete and send this form, together with applicable fee(s), to: Mail** **Mail Stop ISSUE FEE**
**Commissioner for Patents**
**P.O. Box 1450**
**Alexandria, Virginia 22313-1450**
**or Fax (571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25885 7590 08/10/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

**Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| (Depositor's name) |
|---|
| (Signature) |
| (Date) |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | Dale L. Ludwig | X-18524 | 7544 |

TITLE OF INVENTION: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|---|---|---|---|---|---|---|
| nonprovisional | NO | $1510 | $300 | $0 | $1810 | 11/10/2009 |

| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|---|---|---|
| BLANCHARD, DAVID J | 1643 | 530-388150 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1.....

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2.....

3.....

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies .....

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number ..... (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature ..... Date .....

Typed or printed name ..... Registration No. .....

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | Dale L. Ludwig | X-18524 | 7544 |

25885 7590 08/10/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

| EXAMINER | |
|---|---|
| BLANCHARD, DAVID J | |
| ART UNIT | PAPER NUMBER |
| 1643 | |

DATE MAILED: 08/10/2009

**Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)**
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 263 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 263 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

| Notice of Allowability | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/555,407 | LUDWIG, DALE L. | |
| | Examiner | Art Unit | |
| | David J. Blanchard | 1643 | |

***-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--***

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *28 May 2009*.

2. ☒ The allowed claim(s) is/are *12-14,23-34, 41-49 and 57-60 (renumbered as claims 1-28)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   **Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date See Continuation Sheet
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/David J Blanchard/
Primary Examiner, Art Unit 1643

Continuation of Attachment(s) 3. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date: 12/23/08 (3 pages); 12/23/08 (8 pages).

## DETAILED ACTION

1. Claims 1-11, 15-22, 35-40 and 50-56 are cancelled.

   Claims 12-14, 23-27 and 30 have been amended.

   Claims 57-60 have been added.

2. Claims 12-14, 23-34, 41-49 and 57-60 are pending.

### *Election/Restrictions*

3. Applicant`s election of the Invention of Group I, claims 12-14, 23-33 and newly added claims 57-60 in the reply filed on 28 may 2009 is acknowledged.

4. Claim 34 and 41-49 directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 34 and 41-49, directed to the process of making or using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104. Cancelled claims 19-22 (Group II), 34 and 36-40 (Groups III, IV and V), directed to the invention(s) of nucleic acids, vectors and host cells encoding a human antibody or fragment thereof that binds IGF-IR (Group I) and methods of treating acromegaly, retinal neovascularization and psoriasis comprising administering a human antibody or fragment thereof that binds IGF-IR (Groups III, IV and V, respectively) have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement among groups I and VI as set forth in the Office action mailed on 28 April 2009 is hereby WITHDRAWN. For clarity, it is noted that the restriction requirement among groups II, III, IV and V as set forth in the Office action mailed on 28 April 2009 is MAINTAINED**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

***Information Disclosure Statement***

5. The Information Disclosure Statement (IDS) filed 23 December 2008 (3 pages) and 23 December 2008 (twelve pages) have been considered by the Examiner. A signed and initialed copy of each IDS is included with the instant Office Action.

**Examiner's Amendment**

6. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Sanjay M. Jivraj on 29 July 2009

**The claims are amended as follows:**

12. (Currently Amended) An isolated human antibody or fragment thereof, which specifically binds to insulin-like growth factor-I receptor (IGF-IR) comprising complementarity-determining ~~region (CDR)~~ regions (CDRs) having the amino acid sequence SEQ ID NO:14 at $V_H$CDR1, SEQ ID NO:16 at $V_H$CDR2, SEQ ID NO:18 at $V_H$CDR3, SEQ ID NO:20 or 26 at $V_L$CDR1, SEQ ID NO:22 or 28 at $V_L$CDR2, and SEQ ID NO:24 or 30 at $V_L$CDR3.

13. (Currently Amended) The antibody or ~~antigen-binding~~ fragment thereof of Claim 12, which comprises SEQ ID NO:14 at $V_H$CDR1, SEQ ID NO:16 at $V_H$CDR2, SEQ ID NO:18 at $V_H$CDR3, SEQ ID NO:20 at $V_L$CDR1, SEQ ID NO:22 at $V_L$CDR2, and SEQ ID NO:24 at $V_L$CDR3.

14. (Currently Amended) The antibody or ~~antigen-binding~~ fragment thereof of Claim 12, which comprises SEQ ID NO:14 at $V_H$CDR1, SEQ ID NO:16 at $V_H$CDR2, SEQ ID NO:18 at $V_H$CDR3, SEQ ID NO:26 at $V_L$CDR1, SEQ ID NO:28 at $V_L$CDR2, and SEQ ID NO:30 at $V_L$CDR3.

Claims 15-22 (Cancelled)

23. (Currently Amended) A pharmaceutical composition comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 and a pharmaceutically acceptable carrier.

24. (Currently Amended) A conjugate comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 linked to a cytotoxic agent.

25. (Currently Amended) A conjugate comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 linked to a label.

26. (Currently Amended) A therapeutic composition effective to inhibit growth of human tumor cells that express IGF-IR, which composition comprises the antibody or ~~antigen binding~~ fragment thereof of Claim 12.

27. (Currently Amended) The therapeutic composition of Claim 26, which further comprises an antineoplastic agent.

28. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

29. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

30. (Currently Amended) A therapeutic composition effective to promote regression of human tumors that express IGF-IR, which composition comprises the antibody or ~~antibody~~ fragment thereof of Claim 12.

31. (Original) The therapeutic composition of Claim 30, which further comprises an antineoplastic agent.

32. (Original) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

33. (Currently Amended) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, [[or]] and etoposide.

34. (Currently Amended) A method of neutralizing the activation of [[IGF-LR]] IGF-IR, which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of Claim 12

Claims 35-40 (Cancelled)

41. (Currently Amended) A method of reducing tumor growth which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of Claim 12.

42. (Original) The method of Claim 41, which further comprises administering an effective amount of an anti-neoplastic agent.

43. (Original) The method of Claim 42, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

44. (Original) The method of Claim 42, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

45. (Currently Amended) A method of promoting tumor regression which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of

Claim 12.

46. (Original) The method of Claim 45, which further comprises administering an effective amount of an anti-neoplastic agent.

47. (Original) The method of Claim 46, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

48. (Original) The method of Claim 46, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

49. (Original) The method of any one of Claims 41 to 48, wherein the tumor is a breast tumor, colorectal tumor, pancreatic tumor, ovarian tumor, lung tumor, prostate tumor, bone or soft tissue sarcoma or myeloma.

Claims 50-56 (Cancelled)

57. (Currently Amended) An ~~antibody~~ isolated human antibody or fragment thereof comprising [[a]] the heavy chain variable domain ~~represented by~~ of SEQ ID NO:2 and [[a]] the light chain variable domain ~~represented by~~ of SEQ ID NO:6.

58. (Currently Amended) An ~~antibody~~ isolated human antibody or fragment thereof comprising [[a]] the heavy chain variable domain ~~represented by~~ of SEQ ID NO:2 and [[a]] the light chain variable domain ~~represented by~~ of SEQ ID NO:10.

59. (Currently Amended) The antibody of ~~Claims 57-58~~ Claims 57 or 58, wherein said antibody has an IgG1 isotype.

60. (Currently Amended) A pharmaceutical composition comprising the antibody of ~~Claims 57-59~~ Claims 57 or 58 and a pharmaceutically acceptable carrier.

**Amendments to the specification**

On page 1, please delete paragraph [0001] and replace it with the following paragraph:

[0001] This application claims ~~the benefit of United States Provisional Application 60/467,177, filed May 1, 2003~~ priority of and is a U.S. national phase application of PCT/US2004/013852, filed May 3, 2004, which claims priority of U.S. Provisional Application No. 60/467,177, filed May 1, 2003.

Please Amend Paragraphs 15-26 on pages 6 and 7 as follows;

[0015] Figure 1 depicts the nucleotide sequence of the 2F8 heavy chain variable domain (SEQ ID NO:1).

[0016] Figure 2 depicts the amino acid sequence of the 2F8 heavy chain variable domain. CDRs are in bold and underlined (SEQ ID NO:2).

[0017] Figure 3 depicts the nucleotide sequence of the complete 2F8 heavy chain (underline: secretory signal sequence; italics: IgG1 constant region) (SEQ ID NO:3).

[0018] Figure 4 depicts the amino acid sequence of the complete 2F8 heavy chain (underline: secretory signal sequence; bold: CDRs; italics: IgG1 constant region) (SEQ ID NO:4).

[0019] Figure 5 depicts the nucleotide sequence of the 2F8 light chain variable domain (SEQ ID NO:5).

[0020] Figure 6 depicts the amino acid sequence of the 2F8 light chain variable domain. CDRs are in bold and underlined (SEQ ID NO:6).

[0021] Figure 7 depicts the nucleotide sequence of the complete 2F8 light chain (underline: secretory signal sequence; italics: IgG1 constant region) (SEQ ID NO:7).

[0022] Figure 8 depicts the amino acid sequence of the complete 2F8 light chain (underline: secretory signal sequence; bold: CDRs; italics: IgG1 constant region) (SEQ ID NO:8).

[0023] Figure 9 depicts the nucleotide sequence of the A12 light chain variable domain (SEQ ID NO:9).

[0024] Figure 10 depicts the amino acid sequence of the Al2 light chain variable domain. CDRs are in bold and underlined (SEQ ID NO:10).

[0025] Fig. 11 depicts the nucleotide sequence of the complete A12 light chain (underline: secretory signal sequence; italics: IgGl constant region) (SEQ ID NO:11).

[0026] Figure 12 depicts the amino acid sequence of the complete A12 light chain (underline: secretory signal sequence; bold: CDRs; italics: IgGl constant region) (SEQ ID NO:12).

Please Amend Paragraph 81 on page 18 as follows;

[0081] In another embodiment, the present antibodies, or fragments thereof, can have a heavy chain variable region of ~~SEQ ID NO: 1~~ SEQ ID NO: 2 and/or a light chain variable region selected from ~~SEQ ID NO:5 or SEQ ID NO:6~~ SEQ ID NO:6 or SEQ ID NO:10. IMC-A12 is a particularly preferred antibody of the present invention. This antibody has human $V_H$ and $V_L$ framework regions (FWs) as well as CDRs. The $V_H$ variable domain of IMC-A12 (~~SEQ ID NO:1~~ SEQ ID NO:2) has three CDRs corresponding to SEQ ID NOs:14, 16, and 18 and the $V_L$ domain (~~SEQ ID NO:5~~ SEQ ID NO:10) has three CDRs corresponding to ~~SEQ ID NOS:20, 22, and 24~~ SEQ ID NOS:26, 28, and 30. IMC-2F8 is another preferred antibody of the present invention. This antibody also has human $V_H$ and $V_L$ framework regions (FWs) and CDRs. The $V_H$ variable domain of IMC-2F8 is identical to the $V_H$ variable domain of IMCA12. The $V_L$ domain of IMC-2F8 (~~SEQ ID NO:9~~ SEQ ID NO:6) has three CDRs corresponding to ~~SEQ ID NOS:26, 28, and 30~~ SEQ ID NOS:20, 22, and 24.

**Examiner's Statement of Reasons for Allowance**

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Claims 12-14, 23-33 and 57-60 are free of the prior art. The prior art does not teach or fairly suggest an isolated human antibody or fragment thereof comprising the recited heavy and light chain CDR sequences or an antibody comprising the heavy chain variable domain of SEQ ID NO:2 and the light chain variable domain of SEQ ID NO:6 or 10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643

# Exhibit 7

# PART B - FEE(S) TRANSMITTAL

**Complete and send this form, together with applicable fee(s), to:** Mail **Mail Stop ISSUE FEE**
**Commissioner for Patents**
**P.O. Box 1450**
**Alexandria, Virginia 22313-1450**
or Fax **(571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25985 7590 05/10/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

**Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 06/08/2007 | Dale L. Ludwig | X-18524 | 3544 |

TITLE OF INVENTION: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEES DUE | DATE DUE |
|---|---|---|---|---|---|---|
| nonprovisional | NO | $1510 | $300 | $0 | $1810 | 11/10/2009 |

| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|---|---|---|
| BLANCHARD, DAVID J | 1643 | 530-388150 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Sanjay M. Jivraj

2

3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

ImClone, LLC

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

New York, New York

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☒ Issue Fee

☒ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 05-0840 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date NOV 9th 2009

Typed or printed name Sanjay M. Jivraj Registration No. 61,806

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# Electronic Patent Application Fee Transmittal

| | |
|---|---|
| **Application Number:** | 10555407 |
| **Filing Date:** | 08-Jun-2007 |
| **Title of Invention:** | FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR |
| **First Named Inventor/Applicant Name:** | Dale L. Ludwig |
| **Filer:** | Sanjay M. Jivraj/Linda Durbin |
| **Attorney Docket Number:** | X-18524 |

Filed as Large Entity

## U.S. National Stage under 35 USC 371 Filing Fees

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| **Basic Filing:** | | | | |
| **Pages:** | | | | |
| **Claims:** | | | | |
| **Miscellaneous-Filing:** | | | | |
| **Petition:** | | | | |
| **Patent-Appeals-and-Interference:** | | | | |
| **Post-Allowance-and-Post-Issuance:** | | | | |
| Utility Appl issue fee | 1501 | 1 | 1510 | 1510 |
| Publ. Fee- early, voluntary, or normal | 1504 | 1 | 300 | 300 |

| Description | Fee Code | Quantity | Amount | Sub-Total in USD($) |
|---|---|---|---|---|
| Extension-of-Time: | | | | |
| Miscellaneous: | | | | |
| | | | **Total in USD ($)** | **1810** |

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 6422201 |
| **Application Number:** | 10555407 |
| **International Application Number:** | |
| **Confirmation Number:** | 7544 |
| **Title of Invention:** | FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR |
| **First Named Inventor/Applicant Name:** | Dale L. Ludwig |
| **Customer Number:** | 25885 |
| **Filer:** | Sanjay M. Jivraj/Linda Durbin |
| **Filer Authorized By:** | Sanjay M. Jivraj |
| **Attorney Docket Number:** | X-18524 |
| **Receipt Date:** | 10-NOV-2009 |
| **Filing Date:** | 08-JUN-2007 |
| **Time Stamp:** | 05:58:15 |
| **Application Type:** | U.S. National Stage under 35 USC 371 |

## Payment information:

| | |
|---|---|
| Submitted with Payment | yes |
| Payment Type | Deposit Account |
| Payment was successfully received in RAM | $1810 |
| RAM confirmation Number | 6599 |
| Deposit Account | 050840 |
| Authorized User | |

## File Listing:

| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| 1 | Issue Fee Payment (PTO-85B) | X18524IssueFeeTransmittal.pdf | 367132 | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 2 | Fee Worksheet (PTO-875) | fee-info.pdf | 32309 | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | **Total Files Size (in bytes):** | 399441 | | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**
**If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.**

**National Stage of an International Application under 35 U.S.C. 371**
**If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.**

**New International Application Filed with the USPTO as a Receiving Office**
**If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.**

# Exhibit 8

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | ISSUE DATE | PATENT NO. | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/555,407 | 12/29/2009 | 7638605 | X-18524 | 7544 |

25885 7590 12/09/2009

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

# ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

**Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)**
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 263 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Dale L. Ludwig, Randolph, NJ;

# Exhibit 9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant | : Mamoru Watanabe | Art Unit | : 1644 |
| Patent No. | : 7,465,444 | Examiner | : Ilia I. Ouspenski |
| Issue Date | : December 16, 2008 | Conf. No. | : 3057 |
| Serial No. | : 10/472,743 | | |
| 371 date | : March 4, 2004 | | |
| Title | : METHODS OF SUPPRESSING OR TREATING AN INFLAMMATORY BOWEL DISEASE BY ADMINISTERING AN ANTIBODY OR PORTION THEREOF THAT BINDS TO AILIM | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPLICATION FOR PATENT TERM ADJUSTMENT UNDER 37 C.F.R. § 1.705(d)

Patentee hereby requests reconsideration of the Patent Term Adjustment (PTA) accorded the above-referenced patent. Reconsideration of the final PTA calculation to increase total PTA from 653 to 1,322 days, is respectfully requested.

REMARKS

(1) Measuring Overlap of "A Delay" and "B Delay"

"A Delays" are defined as delays by the U.S. Patent and Trademark Office (PTO) under 35 U.S.C. § 154(b)(1)(A), which guarantees prompt PTO response. "B Delays" are defined as delays by the PTO under 35 U.S.C. § 154(b)(1)(B), which guarantees no more than three year application pendency. To the extent that the periods of delay overlap, the period of any term adjustment shall not exceed the actual number of days the issuance of the patent was delayed. 35 U.S.C. § 154(b)(2)(A). As outlined in Wyeth et al. v. Jon W. Dudas (U.S. District Court, D.C., CA No. 07-1492, Mem. Op. September 30, 2008), the only way that these periods of time can "overlap" is if they occur on the same day. If an "A delay" occurs on one calendar day and a "B delay" occurs on another calendar day, they do not overlap and 35 U.S.C. § 154(b)(2)(A) does not limit the extension to one day. Id.

CERTIFICATE OF MAILING BY EFS-WEB FILING

I hereby certify that this paper was filed with the Patent and Trademark Office using the EFS-WEB system on this date: January 8, 2009

The PTA for the instant patent, as currently calculated and shown on the face of the patent, apparently relies on the premise that the application was delayed under 35 U.S.C. § 154(b)(1)(B) *before* the initial three-year period expired. The Wyeth v. Dudas court determined that this construction cannot be squared with the language of 35 U.S.C. § 154(b)(1)(B), which applies "if the issue of an original patent is delayed due to the failure of the United States Patent and Trademark Office to issue a patent within 3 years." "B delay" begins only after the PTO has failed to issue a patent within three years, not before. Id.

(2) Measuring "B Delay" for a National Stage Filing under 35 U.S.C. § 371

In addition to and independent of the "overlap" issue addressed above, Patentee respectfully submits that the Office did not apply the proper standard for determining the period of "B Delay" under 35 U.S.C. § 154(b)(1)(B). It is Patentee's understanding that for purposes of calculating "B Delay," the Office measured application pendency as beginning on March 4, 2004, the date on which the application fulfilled the requirements of 35 U.S.C. § 371. However, as detailed below, the relevant statutes and regulations require that when calculating "B Delay" for a national stage filing under 35 U.S.C. § 371, application pendency must be measured from the date that is 30 months from the priority date of the international application (i.e., not from the date on which the application fulfilled the requirements of 35 U.S.C. § 371).

The term of a patent shall, under certain circumstances, be extended if the Office fails to issue a patent within three years after the "actual filing date" of the application.

> (B) GUARANTEE OF NO MORE THAN 3-YEAR APPLICATION PENDENCY.- Subject to the limitations under paragraph (2), if the issue of an original patent is delayed due to the failure of the United States Patent and Trademark Office to issue a patent within 3 years after the actual filing date of the application in the United States ... the term of the patent shall be extended 1 day for each day after the end of that 3-year period until the patent is issued.
> 35 U.S.C. § 154(b)(1)(B). (emphasis added)

37 C.F.R. § 1.702(b) explains the meaning of the term "actual filing date" as used in 35 U.S.C. § 154(b)(1)(B). As detailed below, PTO delay for a national stage application begins

if the Office fails to issue a patent within three years after the date the national stage "commenced under 35 U.S.C. 371(b) or (f)."[1]

> (b) *Failure to issue a patent within three years of the actual filing date of the application.* Subject to the provisions of 35 U.S.C. 154(b) and this subpart, the term of an original patent shall be adjusted if the issuance of the patent was delayed due to the failure of the Office to issue a patent within three years after the date on which the application was filed under 35 U.S.C. 111(a) or the national stage commenced under 35 U.S.C. 371(b) or (f) in an international application, but not including... 37 C.F.R. § 1.702(b). (emphasis added)

35 U.S.C. §§ 371(b) and (f) refer to the time when a national stage application "commences."

> (b) Subject to subsection (f) of this section, the national stage shall commence with the expiration of the applicable time limit under article 22 (1) or (2), or under article 39 (1)(a) of the treaty. 35 U.S.C. § 371(b). (emphasis added)

> (f) At the express request of the applicant, the national stage of processing may be commenced at any time at which the application is in order for such purpose and the applicable requirements of subsection (c) of this section have been complied with. 35 U.S.C. § 371(f).

35 U.S.C. § 371(f) relates to the situation where an applicant files an express request for early processing of an international application. In the absence of filing such a request, the U.S. national stage commences under the provisions of 35 U.S.C. § 371(b), i.e., with the expiration of the applicable time limit under article 22(1) or (2), or under article 39(1)(a) of the treaty. The term "the treaty" refers to "the Patent Cooperation Treaty done at Washington, on June 19, 1970." See 35 U.S.C. § 351(a).

---

[1] Consistent with 37 C.F.R. § 1.702(b), MPEP § 2730 states that "[i]n the case of an international application, the phrase 'actual filing date of the application in the United States' [as used in 35 U.S.C. § 154(b)(1)(B)] means the date the national stage commenced under 35 U.S.C. 371(b) or (f)."

The articles of the Patent Cooperation Treaty cited in 35 U.S.C. § 371(b) are reproduced below.

**Article 22**

**Copy, Translation, and Fee, to Designated Offices**

(1) The applicant shall furnish a copy of the international application (unless the communication provided for in Article 20 has already taken place) and a translation thereof (as prescribed), and pay the national fee (if any), to each designated Office not later than at the expiration of 30 months from the priority date. Where the national law of the designated State requires the indication of the name of and other prescribed data concerning the inventor but allows that these indications be furnished at a time later than that of the filing of a national application, the applicant shall, unless they were contained in the request, furnish the said indications to the national Office of or acting for the State not later than at the expiration of 30 months from the priority date. (emphasis added)

(2) Where the International Searching Authority makes a declaration, under Article 17(2)(a), that no international search report will be established, the time limit for performing the acts referred to in paragraph (1) of this Article shall be the same as that provided for in paragraph (1).

**Article 39**
**Copy, Translation, and Fee, to Elected Offices**

(1) (a) If the election of any Contracting State has been effected prior to the expiration of the 19th month from the priority date, the provisions of Article 22 shall not apply to such State and the applicant shall furnish a copy of the international application (unless the communication under Article 20 has already taken place) and a translation thereof (as prescribed), and pay the national fee (if any), to each elected Office not later than at the expiration of 30 months from the priority date. (emphasis added)

"The applicable time limit" referred to in Patent Cooperation Treaty articles 22(1), 22(2), and 39(1)(a) is "the expiration of 30 months from the priority date." As a result, "the expiration of 30 months from the priority date" is the time at which the U.S. national stage commences

under the provisions of 35 U.S.C. § 371(b). This same conclusion as to the timing for commencement of the U.S. national stage is also summarized in MPEP § 1893.01.

> Subject to 35 U.S.C. 371(f), commencement of the national stage occurs upon expiration of the applicable time limit under PCT Article 22(1) or (2), or under PCT Article 39(1)(a). See 35 U.S.C. 371(b) and 37 CFR 1.491(a). PCT Articles 22(1), 22(2), and 39(1)(a) provide for a time limit of not later than the expiration of 30 months from the priority date. Thus, in the absence of an express request for early processing of an international application under 35 U.S.C. 371(f) and compliance with the conditions provided therein, the U.S. national stage will commence upon expiration of 30 months from the priority date of the international application. Pursuant to 35 U.S.C. 371(f), the national stage may commence earlier than 30 months from the priority date, provided applicant makes an express request for early processing and has complied with the applicable requirements under 35 U.S.C. 371(c). MPEP § 1893.01. (emphasis added)

In view of the foregoing, the "actual filing date" of a U.S. national stage application filed under 35 U.S.C. § 371, for purposes of calculating "B Delay" under 35 U.S.C. § 154(b)(1)(B) and 37 C.F.R. § 1.702(b), is the date that is 30 months from the priority date of the international application.[2]

## REVIEW OF PATENT TERM ADJUSTMENT CALCULATION

"A Delay"

A first PTO action was due on or before May 4, 2005 (the date that is fourteen months after March 4, 2004, the date on which the application fulfilled the requirements of 35 U.S.C. § 371). The PTO mailed the first non-final Office Action on October 24, 2006, thereby according a PTO Delay of 538 days. Patentee does not dispute the PTO's calculation for this "A Delay" from May 5, 2005 (the day after the date that is fourteen months after the date on

[2] In contrast to reliance on "the expiration of 30 months from the priority date" for measuring "B Delay," the beginning of the relevant period for purposes of calculating "A Delay" is the date on which an international application fulfills the requirements of 35 U.S.C. § 371. See 35 U.S.C. § 154(b)(1)(A)(i)(II)and 37 C.F.R. § 1.702(a)(1).

which the application fulfilled the requirements of 35 U.S.C. § 371), to October 24, 2006. See 37 C.F.R. §§ 1.702(a)(1) and 1.703(a)(1).

In view of the period of "A Delay" detailed above, the total "A Delay" for this patent should be calculated as 538 days.

"B Delay"

The present application is a national stage filing under 35 U.S.C. § 371 of international application number PCT/JP02/01361, filed February 18, 2002, which claims the benefit of priority of Japanese application number 2001-89158, filed March 27, 2001, and Japanese application number 2002-19291, filed January 29, 2002.

The national stage for the present application "commenced" under the provisions of 35 U.S.C. § 371(b), i.e., upon expiration of 30 months from the priority date of the international application.[3] As a result, the date that the national stage commenced was September 27, 2003 (i.e., 30 months from the priority date of March 27, 2001).

The period beginning on September 28, 2006 (the day after the date that is three years after September 27, 2003, the date that the national stage commenced), and ending December 16, 2008 (the date the patent was issued), is 811 days in length.

In view of the period of "B Delay" detailed above, the total "B Delay" for this patent should be calculated as 811 days. The PTO calculated 115 days of delay for issuance of a patent more than three years after filing. Patentee respectfully submits that the PTO's calculation of this "B Delay" is incorrect and that the correct PTO Delay for issuance beyond three years from filing is 811 days. See 37 C.F.R. §§ 1.702(b) and 1.703(b).

[3] No request for early processing under 35 U.S.C. § 371(f) was filed for the present application.

Overlap of "A Delay" and "B Delay"

As detailed above, "A Delay" accumulated during the following period:

May 5, 2005, to October 24, 2006.

As detailed above, "B Delay" accumulated during the following period:

September 28, 2006, to December 16, 2008.

The "A Delay" and the "B Delay" overlap (i.e., occur on the same calendar day) for a total of 27 days, from September 28, 2006, to October 24, 2006.

Applicant Delay

There were no circumstances constituting a failure to engage in reasonable efforts to conclude processing or examination of the application as set forth 37 C.F.R. § 1.704.

Terminal Disclaimer

This patent is not subject to a terminal disclaimer.

Conclusion

In consideration of the events described above, Patentee believes the PTA calculation of 653 days is incorrect. As such, Patentee respectfully requests reconsideration of the PTA in the following manner:

1) Total PTO Delay should be calculated as 1,322 days (i.e., the sum of 538 days of "A Delay" and 811 days of "B Delay" minus the 27 days of overlap);

2) Total Applicant Delay should be calculated as 0 days; and

3) Total PTA should be calculated as 1,322 days.

Please apply the fee of $200 required under 37 C.F.R. § 1.18(e) and any other required charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket Number 14539-0010US1.

Respectfully submitted,

Date: January 8, 2009

Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (877) 769-7945

30464624.doc

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

FISH & RICHARDSON P.C.
P.O. BOX 1022
MINNEAPOLIS MN 55440-1022

COPY MAILED

JUN 16 2009

OFFICE OF PETITIONS

In re Patent No. 7,465,444 :
Mamoru Watanabe :
Issue Date: December 16, 2008 :
Application No. 10/472,743 : DECISION ON REQUEST FOR
Filed: March 24, 2004 : RECONSIDERATION OF
Attorney Docket No. 14539-010US1 : PATENT TERM ADJUSTMENT
Title: Methods Of Suppressing or Treating An Inflammatory Bowel Disease by Administering an Antibody or Portion Thereof That Binds To Ailim :

This is a decision on the "APPLICATION FOR PATENT TERM ADJUSTMENT UNDER 37 C.F.R. § 1.705(d)," filed January 8, 2009.

The application for reconsideration of patent term adjustment is **GRANTED** to the extent indicated herein.

The above-identified application matured into U.S. Patent No. 7,465,444 on December 16, 2008. The patent issued with a patent term adjustment of 653 days. This request for reconsideration of patent term adjustment was timely filed within two months of the issue date of the patent. See, 37 CFR 1.705(d). Patentees request that the patent term adjustment determination for the above-identified patent be changed from 653 days to 1322 days.

Patentee requests recalculation of the patent term adjustment based on the decision in Wyeth v. Dudas, 580 F. Supp. 2d 138, 88 U.S.P.Q. 2d 1538 (D.D.C. 2008). Patentees assert that pursuant to Wyeth, a PTO delay under 35 U.S.C. 154(b)(1)(A) overlaps with a delay under 35 U.S.C. 154(b)(1)(B) only if the delays occur on the same day.

The petition submitted by patentee sets forth a period of adjustment for Office delays totaling 1349 days (Three Year Delay under 37 CFR 1.703(b) of 811 days *plus* a period of adjustment due to examination delay pursuant to 37 CFR 1.702(a) of 538 days). The petition also sets forth an overlap of 27 days. The petition reflects a reduction of patent term adjustment totaling "0" days for applicant's failure to engage in reasonable efforts to conclude prosecution pursuant to 37 CFR 1.704. Thus, patentee asserts entitlement to an overall adjustment of 1322 days (1349(811+538)) days for Office delay *less* 27 days for overlap).

Patentee's petition does not dispute the adjustments under 37 CFR 1.702(a) totaling 538 days. Patentee's petition acknowledges the "0" reductions for applicant's failure to engage in reasonable efforts to conclude prosecution pursuant to 37 CFR 1.704. These reductions total 0 days.

Under 37 CFR 1.703(f), patentees are entitled to a period of patent term adjustment equal to the period of delays based on the grounds set forth in 37 CFR 1.702 reduced by the period of time during which patentees failed to engage in reasonable efforts to conclude prosecution pursuant to 37 CFR 1.704.

The Office agrees that as of the issuance of the patent on December 16, 2008, the application was pending three years and 811 days after the commencement date (September 27, 2003) pursuant to 37 CFR 1.371.The Office agrees that because certain actions were not taken within specified time frames, the patent is entitled to an adjustment of 538 days pursuant to 37 CFR 1.702(a). At issue is whether patentees should accrue an additional 811 days of patent term adjustment for the Office taking in excess of three years to issue the patent, as well as 538 days for Office failure to take a certain action within a specified time frame (or examination delay).

The Office contends that 538 of the 811 days overlap. Patentee's calculation of the period of overlap is inconsistent with the Office's interpretation of this provision. 35 U.S.C. 154(b)(2)(A) limits the adjustment of patent term, as follows:

> To the extent that the periods of delay attributable to grounds specified in paragraph (1) overlap, the period of any adjustment granted under this subsection shall not exceed the actual number of days the issuance of the

patent was delayed.

Likewise, 35 CFR 1.703(f) provides that:

> To the extent that periods of delay attributable to the grounds specified in § 1.702 overlap, the period of adjustment granted under this section shall not exceed the actual number of days the issuance of the patent was delayed.

As explained in Explanation of 37 CFR 1.703(f) and of the United States Patent and Trademark Office Interpretation of 35 U.S.C. 154(b)(2)(A), 69 Fed. Reg. 34283 (June 21, 2004), the Office interprets 35 U.S.C. 154(b)(2)(A) as permitting either patent term adjustment under 35 U.S.C. 154(b)(1)(A)(i)-(iv), or patent term adjustment under 35 U.S.C. 154(b)(1)(B), but not as permitting patent term adjustment under both 35 U.S.C. 154(b)(1)(A)(i)-(iv) and 154(b)(1)(B). Accordingly, the Office implements the overlap provision as follows:

> If an application is entitled to an adjustment under 35 U.S.C. 154(b)(1)(B), the entire period during which the application was pending (except for periods excluded under 35 U.S.C. 154(b)(1)(B)(i)-(iii)), and not just the period beginning three years after the actual filing date of the application or the national stage commenced under 35 U.S.C. 371(b) or (f), is the period of delay under 35 U.S.C. 154(b)(1)(B) in determining whether periods of delay overlap under 35 U.S.C. 154(b)(2)(A). Thus, any days of delay for Office issuance of the patent more than 3 years after the filing or commencement date of the application, which overlap with the days of patent term adjustment accorded prior to the issuance of the patent will not result in any additional patent term adjustment. See, 35 U.S.C. 154(b)(1)(B), 35 U.S.C. 154(b)(2)(A), and 37 CFR § 1.703(f). See, Changes to Implement Patent Term Adjustment Under Twenty Year Term; Final Rule, 65 Fed. Reg. 56366 (Sept. 18, 2000). See, also, Revision of Patent Term Extension and Patent Term Adjustment Provisions; Final Rule, 69 Fed. Reg. 21704 (April 22, 2004), 1282 Off. Gaz. Pat. Office 100 (May 18, 2004). See, also, Explanation of 37 CFR 1.703(f) and of the United States Patent and Trademark Office Interpretation of 35 U.S.C. 154(b)(2)(A), 69 Fed. Reg. 34283 (June 21, 2004).

The current wording of § 1.703(f) was revised in response to the misinterpretation of this provision by a number of Patentees. The rule was slightly revised to more closely track the corresponding language of 35 U.S.C. 154(b)(2)(A). The relevant portion differs only to the extent that the statute refers back to provisions of the statute whereas the rule refers back to sections of the rule. This was not a substantive change to the rule nor did it reflect a change of the Office's interpretation of 35 U.S.C. 154(b)(2)(A). As stated in the Explanation of 37 CFR 1.703(f) and of the United States Patent and Trademark Office Interpretation of 35 U.S.C. 154(b)(2)(A), the Office has consistently taken the position that if an application is entitled to an adjustment under the three-year pendency provision of 35 U.S.C. 154(b)(1)(B), the entire period during which the application was pending before the Office (except for periods excluded under 35 U.S.C. 154(b)(1)(B)(i)-(iii)), and not just the period beginning three years after the actual filing date of the application or the national stage commenced under 35 U.S.C. 371(b) or (f), is the relevant period under 35 U.S.C. 154(b)(1)(B) in determining whether periods of delay "overlap" under 35 U.S.C. 154(b)(2)(A).

This interpretation is consistent with the statute. Taken together the statute and rule provide that to the extent that periods of delay attributable to grounds specified in 35 U.S.C. 154(b)(1) and in corresponding § 1.702 overlap, the period of adjustment granted shall not exceed the actual number of days the issuance of the patent was delayed. The grounds specified in these sections cover the A) guarantee of prompt Patent and Trademark Office responses, B) guarantee of no more than 3-year application pendency, and C) guarantee or adjustments for delays due to interference, secrecy orders and appeals. A section by section analysis of 35 U.S.C. 154(b)(2)(A) specifically provides that:

> Section 4402 imposes limitations on restoration of term. In general, pursuant to [35 U.S.C.] 154(b)(2)(A)-(C), total adjustments granted for restorations under [35 U.S.C. 154](b)(1) are reduced as follows: (1) To the extent that there are multiple grounds for extending the term of a patent that may exist simultaneously (e.g., delay due to a secrecy order under [35 U.S.C.] 181 and administrative delay under [35 U.S.C.] 154(b)(1)(A)), the term should not be extended for each ground of delay but only for the

actual number of days that the issuance of a patent was delayed; See 145 Cong. Rec. S14,718[1]

As such, the period for over three-year pendency does not overlap only to the extent that the actual dates in the period beginning three years after the date on which the application commenced overlap with the actual dates in the periods for failure of the Office to take action within specified time frames. In other words, consideration of the overlap does not begin three years after the commencement date of the application.

In this instance, the relevant period under 35 U.S.C. 154(b)(1)(B) in determining whether periods of delay "overlap" under 35 U.S.C. 154(b)(2)(A) is the entire period during which the application was pending before the Office

The application actually issued three years and 811 days after its commencement date. The Office did not delay 538 days and then delay an additional 811 days.

Accordingly, the proper adjustment of 811 days of patent term adjustment (not 538 days and 811 days) should have been entered because the period of delay of 538 of 811 days attributable to the delay in the issuance of the patent overlaps with the adjustment of 538 days attributable to grounds specified in § 1.702(a). Entry of both periods is not warranted. Thus, 811 days is determined to be the actual number of days that the issuance of the patent was delayed.

In view thereof, the patent term adjustment indicated in the patent should have been eight hundred eleven **(811)** days.

Receipt of the $200.00 fee set forth in 37 CFR 1.18(e) is acknowledged. No additional fees are required.

Patentees are given THIRTY (30) DAYS or ONE (1) MONTH, whichever is longer, from the mail date of this decision to respond to

---

[1] The AIPA is title IV of the Intellectual Property and Communications Omnibus Reform Act of 1999 (S. 1948), which was incorporated and enacted as law as part of Pub. L. 106-113. The Conference Report for H.R. 3194, 106th Cong. 1st Sess. (1999), which resulted in Pub. L. 106-113, does not contain any discussion (other than the incorporated language) of S. 1948. A section-by-section analysis of S. 1948, however, was printed in the Congressional Record at the request of Senator Lott, See 145 Cong. Rec. S14,708-26 (1999)(daily ed. Nov. 17, 1999).

this decision. No extensions of time will be granted under § 1.136.

The application will be forwarded to the Certificates of Correction Branch for issuance of a certificate of correction in order to rectify this error. See 35 U.S.C. § 254 and 37 CFR§ 1.322. After the thirty day time period has elapsed, the Office will sua sponte issue a certificate of correction indicating that the term of the above-identified patent is extended or adjusted by eight hundred eleven **(811)** days.

Kery A. Fries

Kery Fries
Senior Legal Advisor Attorney
Office of Patent Legal Administration

Cc: Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, NY 10022-4611